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DATE: Wednesday, January 09, 2008

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		DB=PGPB,USPT; PLUR=YES; OP=OR	
☐	L1	corticotropin adj releasing adj hormone adj receptor adj 2 adj agonist or corticotropin adj releasing adj hormone adj receptor adj 1 adj antagonist	18

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                   MEDLINE segment
 NEWS 26  DEC 17   MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
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=> s corticotropin(w)releasing(w)hormone(w)receptor(w)2(w)agonist or cortocotropin(w)releasing(w)hormone(w)receptor(w)1(w)antagonist
L1 0 CORTICOTROPIN(W) RELEASING(W) HORMONE(W) RECEPTOR(W) 2(W) AGONIST OR CORTOCOTROPIN(W) RELEASING(W) HORMONE(W) RECEPTOR(W) 1(W) ANTAGONIST

=> s corticotropin(w)releasing(w)hormone(w)receptor(w)2 or cortocotropin(w)releasing(w)hormone(w)receptor(w)1
L2 106 CORTICOTROPIN(W) RELEASING(W) HORMONE(W) RECEPTOR(W) 2 OR CORTOCOTROPIN(W) RELEASING(W) HORMONE(W) RECEPTOR(W) 1

=> s l2 and (agonist or antagonist)
L3 17 L2 AND (AGONIST OR ANTAGONIST)

=> s l3 and inflammation
L4 6 L3 AND INFLAMMATION

=> dup rem l3
PROCESSING COMPLETED FOR L3
L5 14 DUP REM L3 (3 DUPLICATES REMOVED)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L6 3 DUP REM L4 (3 DUPLICATES REMOVED)

=> dis ibib abs l5 1-14

L5 ANSWER 1 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:217737 BIOSIS
DOCUMENT NUMBER: PREV200700218245
TITLE: Corticotropin-releasing hormone receptor (CRHR)1 and CRHR2 are both trafficking and signaling receptors for urocortin.
AUTHOR(S): Tu, Hong; Kastin, Abba J.; Pan, Weihong [Reprint Author]
CORPORATE SOURCE: Pennington Biomed Res Ctr, 6400 Perkins Rd, Baton Rouge, LA

70808 USA
weihong.pan@pbrc.edu
SOURCE: Molecular Endocrinology, (MAR 2007) Vol. 21, No. 3, pp. 700-711.
CODEN: MOENEN. ISSN: 0888-8809.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2007
Last Updated on STN: 28 Mar 2007
AB Transport of urocortin, a potent satiety peptide, occurs at the blood-brain barrier of the mouse. Endocytosis of urocortin by the cerebral microvessel endothelial cells composing the blood-brain barrier is a rate-limiting step of this transport, but the cellular mechanisms involved have not been fully elucidated. The presence of both CRH receptors R1 and R2 in isolated cerebral microvessels shown in this study suggested that both subtypes might mediate urocortin transport. The roles of these two receptors in the endocytosis and signal transduction of urocortin were tested by overexpression studies in human embryonic kidney 293 cells. Both receptors led to a significant increase of binding and endocytosis of radiolabeled urocortin. CRHR1-mediated urocortin endocytosis was blocked by astressin (antagonist for both CRHRs), whereas CRHR2-mediated urocortin endocytosis was also blocked by antisauvagine 30 (selective CRHR2 beta antagonist). Chlorpromazine, filipin, and nystatin had no effect on urocortin endocytosis, indicating the lack of significant involvement of clathrin or caveolae membrane microdomains. Both CRHR1 and CRHR2 were able to mediate the ligand-induced increase of cAMP production, suggesting that the overexpressed receptors were biologically active. Elevation of intracellular cAMP by forskolin or dibutyryl-cAMP, however, did not show acute modulation of the binding and endocytosis of urocortin. Despite the substantial intracellular degradation of endocytosed urocortin in cells overexpressing either CRHR1 or CRHR2, intact urocortin could be exocytosed during the 1-h study interval. We conclude that both CRHR1 and CRHR2 play a facilitatory role in the non-clathrin-, non-caveolae-mediated endocytosis and intracellular signal transduction of this potent peptide.

L5 ANSWER 2 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:585328 BIOSIS.
DOCUMENT NUMBER: PREV200700586297
TITLE: Intratumoral CRH modulates immuno-escape of ovarian cancer cells through FasL regulation.
AUTHOR(S): Minas, V.; Rolaki, A.; Kalantaridou, S. N.; Sidiropoulos, J.; Mitrou, S.; Petsas, G.; Jeschke, U.; Paraskevaidis, E. A.; Fountzilas, G.; Chrousos, G. P.; Pavlidis, N.; Makrigiannakis, A. [Reprint Author]
CORPORATE SOURCE: Univ Crete, Fac Med, Dept Obstet and Gynecol, Lab Human Reprod, GR-71003 Iraklion, Greece
makrigia@med.uoc.gr
SOURCE: British Journal of Cancer, (AUG 28 2007) Vol. 97, No. 5, pp. 637-645.
CODEN: BJCAAI. ISSN: 0007-0920. E-ISSN: 1532-1827.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 2007
Last Updated on STN: 21 Nov 2007
AB Although corticotropin-releasing hormone (CRH) and Fas ligand (FasL) have been documented in ovarian carcinoma, a clear association with tumour progression and immuno-escape has not been established. FasL plays an important role in promoting tumour cells' ability to counterattack immune cells. Here, we examined immunohistochemically the expression of CRH, CRHR1,CRHR2 and FasL in 47 human ovarian cancer cases. The ovarian cancer cell lines OvCa3 and A2780 were further used to test the hypothesis that CRH might contribute to the immune privilege of ovarian tumours, by modulating FasL expression on the cancer cells. We found that CRH, CRHR1,

CRHR2 and FasL were expressed in 68.1, 70.2, 63.8 and 63.8% of the cases respectively. Positivity for CRH or FasL expression was associated with higher tumour stage. Finally, CRH increased the expression of FasL in OvCa3 and A2780 cells through CRHR1 thereby potentiated their ability to induce apoptosis of activated peripheral blood lymphocytes. Corticotropin-releasing hormone produced by human ovarian cancer might favour survival and progression of the tumour by promoting its immune privilege. These findings support the hypothesis that CRHR1 antagonists could potentially be used against ovarian cancer.

L5 ANSWER 3 OF 14 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2006495694 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16920976
TITLE: Corticotropin-releasing hormone receptor 2-deficient mice have reduced intestinal inflammatory responses.
AUTHOR: Kokkotou Efi; Torres Daniel; Moss Alan C; O'Brien Michael; Grigoriadis Dimitri E; Karalis Katia; Pothoulakis Charalabos
CORPORATE SOURCE: Gastrointestinal Neuropeptide Center, Gastroenterology Division, Beth Israel Deaconess Medical Center, Boston, MA 02215, USA.
CONTRACT NUMBER: DK 38458 (NIDDK)
DK 47977 (NIDDK)
P0-1 DK 33506 (NIDDK)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2006 Sep 1) Vol. 177, No. 5, pp. 3355-61.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 22 Aug 2006
Last Updated on STN: 6 Oct 2006
Entered Medline: 5 Oct 2006

AB Corticotropin-releasing hormone (CRH) and urocortins (Ucn) bind with various affinities to two G-protein-coupled receptors, CRHR1 and CRHR2, which are expressed in brain and in peripheral tissues, including immune cells. CRHR2-deficient mice display anxiety-like behavior, hypersensitivity to stress, altered feeding behavior and metabolism, and cardiovascular abnormalities. However, the phenotype of these mice in inflammatory responses has not been determined. In the present study we found that compared with wild-type CRHR2-null mice developed substantially reduced intestinal inflammation and had lower intestinal mRNA expression of the potent chemoattractants keratinocyte chemokine and monocyte chemoattractant protein 1 following intraluminal exposure to Clostridium difficile toxin A, a potent enterotoxin that mediates antibiotic-associated diarrhea and colitis in humans. This effect was recapitulated by administration of astressin 2B, a selective CRHR2 antagonist, before toxin A exposure. Moreover, Ab array analysis revealed reduced expression of several inflammatory chemokines, including keratinocyte chemokine and monocyte chemoattractant protein 1 in toxin A-exposed mice pretreated with astressin 2B. Real-time RT-PCR of wild-type mouse intestine showed that only UcnII, but not other Ucn, was significantly up-regulated by ileal administration of toxin A at 4 h compared with buffer exposure. We also found that human colonic epithelial HT-29 cells express CRHR2alpha mRNA, whereas expression of beta and gamma spliced variants was minimal. Moreover, treatment of HT-29 cells with UcnII, which binds exclusively to CRHR2, stimulated expression of IL-8 and monocyte chemoattractant protein 1. Taken together, these results provide direct evidence that CRHR2 mediates intestinal inflammatory responses via release of proinflammatory mediators at the colonocyte level.

L5 ANSWER 4 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:528803 BIOSIS
DOCUMENT NUMBER: PREV200600523423
TITLE: Research on the effect of corticotropin-releasing hormone receptors in stress reaction.
AUTHOR(S): Zeng Chun [Reprint Author]; Yan Can; Xu Zhi-wei; Wu Li-li
CORPORATE SOURCE: Guangzhou Univ TCM, Basic Med Coll, Guangzhou 510405, Peoples R China
zengchun56@tom.com
SOURCE: Zhongguo Yaolixue Tongbao, (MAY 2006) Vol. 22, No. 5, pp. 517-520.
ISSN: 1001-1978.
DOCUMENT TYPE: Article
LANGUAGE: Chinese
ENTRY DATE: Entered STN: 12 Oct 2006
Last Updated on STN: 12 Oct 2006

AB Corticotropin-releasing hormone (CRH) is the key regulator during stress reaction which integrates endocrine, autonomic, immune and behavioral responses to stressors. Receptors mediating the action of CRH have been identified as CRH-R1, CRH-R2 and CRH-R3. In the process of stress reaction, CRH mainly interacts with CRH-R1 and CRH-R2, producing multiple physiological and pathological effects. In recent years, by employing transgenic animals, selective CRH-receptor antagonists and special CRH-receptor agonists, the effect of CRH receptors on stress reaction and its mechainisms have been deeply realized.

L5 ANSWER 5 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:439439 BIOSIS
DOCUMENT NUMBER: PREV200600440304
TITLE: The molecular mechanisms underlying the regulation of the biological activity of corticotropin-releasing hormone receptors: Implications for physiology and pathophysiology.
AUTHOR(S): Hillhouse, Edward W. [Reprint Author]; Grammatopoulos, Dimitris K.
CORPORATE SOURCE: Univ Leeds, Leeds Inst Genet Hlth and Therapeut, Leeds LS2 9NL, W Yorkshire, UK
e.w.hillhouse@leeds.ac.uk; d.grammatopoulos@warwick.ac.uk
SOURCE: Endocrine Reviews, (MAY 2006) Vol. 27, No. 3, pp. 260-286.
CODEN: ERVIDP. ISSN: 0163-769X.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Sep 2006
Last Updated on STN: 6 Sep 2006

AB The CRH receptor (CRH-R) is a member of the secretin family of G protein-coupled receptors. Wide expression of CRH-Rs in the central nervous system and periphery ensures that their cognate agonists , the family of CRH-like peptides, are capable of exerting a wide spectrum of actions that underpin their critical role in integrating the stress response and coordinating the activity of fundamental physiological functions, such as the regulation of the cardiovascular system, energy balance, and homeostasis. Two types of mammal CRH-R exist, CRH-R1 and CRH-R2, each with unique splicing patterns and remarkably distinct pharmacological properties, but similar signaling properties, probably reflecting their distinct and sometimes contrasting biological functions. The regulation of CRH-R expression and activity is not fully elucidated, and we only now begin to fully understand the impact on mammalian pathophysiology. The focus of this review is the current and evolving understanding of the molecular mechanisms controlling CRH-R biological activity and functional flexibility. This shows notable tissue-specific characteristics, highlighted by their ability to couple to distinct G proteins and activate tissue-specific signaling cascades. The type of activating agonist, receptor, and target cell appears to play a

major role in determining the overall signaling and biological responses in health and disease.

L5 ANSWER 6 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:78987 BIOSIS
DOCUMENT NUMBER: PREV200700077289
TITLE: Neuropeptide urocortin and its receptors are expressed in rat Kupffer cells.
AUTHOR(S): Charalampopoulos, Ioannis; Androulidaki, Ariadne; Minas, Vassilis; Chatzaki, Ekaterini; Tsatsanis, Chistos; Notas, George; Xidakis, Costas; Kolios, George; Kouroumalis, Elias; Margioris, Andrew N.; Gravanis, Achille [Reprint Author]
CORPORATE SOURCE: Univ Crete, Sch Med, Dept Pharmacol, GR-71110 Iraklion, Greece
gravanis@med.uoc.gr
SOURCE: Neuroendocrinology, (2006) Vol. 84, No. 1, pp. 49-57.
CODEN: NUNDAJ. ISSN: 0028-3835.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jan 2007
Last Updated on STN: 24 Jan 2007

AB The stress neuropeptides, corticotropin-releasing hormone (CRH) and urocortin (UCN), modulate the inflammatory response via the hypothalamus-pituitary-adrenal axis and locally, in a paracrine manner, act on mast and macrophage cells. Kupffer cells (KCs) are the resident macrophages of the liver. They represent the bulk of tissue macrophages in the body and they are the first to face invading noxious agents reaching the body via the portal circulation. The aim of the present report was to study the expression of the CRH system in rat KC and test its functionality. Our findings are as follows: (1) In highly purified KCs the transcripts of UCN, of its receptors CRHR1, CRHR2 and that of the pseudoreceptor CRH-binding protein (CRHBP) were present while that of CRH was not detectable. (2) Similarly, immunoreactive UCN, CRHR1, CRHR2 and CRHBP were easily detectable by immunohistochemistry and immunofluorescence in sections of whole rat liver (localized in KC) as well as in purified KC while CRH was again not detectable. (3) Exposure of purified KC to CRH or UCN suppressed lipopolysaccharide-induced tumor necrosis factor alpha production, an effect completely prevented by the CRHR1 and CRHR2 receptor antagonist astressin. Our data demonstrate the presence of UCN and its receptors in rat KC, the absence of CRH, and the functionality of these receptors. We propose that a UCN-based system may affect local inflammatory phenomena in the liver acting in a paracrine manner. Copyright (c) 2006 S. Karger AG, Basel.

L5 ANSWER 7 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:534806 BIOSIS
DOCUMENT NUMBER: PREV200510320309
TITLE: Human umbilical cord blood-derived mast cells (hCBMCs) express multiple isoforms of corticotropin-releasing hormone (CRH) receptors.
AUTHOR(S): Cao, Jing [Reprint Author]; Papadopoulou, Nikoletta; Kempuraj, Duraisamy; Theoharides, Theoharis C.
CORPORATE SOURCE: Tufts Univ, Sch Med, Dept Biochem and Pharamcol, Medford, MA 02155 USA
SOURCE: FASEB Journal, (MAR 7 2005) Vol. 19, No. 5, Suppl. S, Part 2, pp. A1417.
Meeting Info.: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences. San Diego, CA, USA. March 31 -April 06, 2005. Amer Assoc Anatomists; Amer Assoc Immunologists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr Sci; Amer Soc Pharmacol & Expt Therapeut; Int Union Physiol Sci.

CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Dec 2005
Last Updated on STN: 1 Dec 2005

AB CRH, produced mainly in the brain, is a key regulator of the hypothalamic-pituitary-adrenal (HPA) axis and the response to stress. CRH is also secreted peripherally and has proinflammatory effects, apparently through activation of mast cells. CRH exerts its effects by binding to two receptor subtypes, CRHR1 andCRHR2, activating adenylate cyclase, with increased cAMP production. So far, a direct effect of CRH on mast cells has not been documented. We previously identified a number of CRHR1 isoforms (1 alpha, 1 beta, 1c, 1e, 1f and 1g) in human leukemic mast cells (HMC-1); CRH activated CRHR1, leading to elevated cAMP. Here, we investigated whether CRH receptor subtypes are also expressed in normal hCBMCs by RT-PCR. We showed for the first time that hCBMCs express multiple CRHR1 isoforms (1 alpha, 1 beta, 1c, 1e, 1f), with 1d and 1g being absent. Interestingly, CRHR2 alpha, but not 2 beta or 2 gamma, was detected by RT-PCR.Moreover, CRHR1 activation by CRH led to significantly increased cAMP, which could be blocked by the specific CRHR1 antagonist Antalarmin; CRHR2 activationby CRH-related peptides urocortin (Ucn), Ucn II or III also significantly increased cAMP in hCBMCs, which could be inhibited by the specific CRER2 antagonist Astressin 2B. The diversity of CRHR isoforms expressed in human mast cells and the recently reported ability of mast cells to synthesize and secrete CRH/Ucn suggest that these peptides may have different autocrine effects.

L5 ANSWER 8 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:48880 BIOSIS
DOCUMENT NUMBER: PREV200500050329
TITLE: Behavioral, adrenal, and sympathetic responses to long-term administration of an oral corticotropin-releasing hormone receptor antagonist in a primate stress paradigm.
AUTHOR(S): Ayala, Alejandro R. [Reprint Author]; Pushkas, Judy; Higley, J. Dee; Ronsaville, Donna; Gold, Philip W.; Chrousos, George P.; Pacak, Karel; Calis, Karim A.; Gerald, Melissa; Lindell, Stephen; Rice, Kenner C.; Cizza, Giovanni
CORPORATE SOURCE: Bldg 10,Room 9D-42,10 Ctr Dr, Bethesda, MD, 20892, USA
ayalaa@nih.gov
SOURCE: Journal of Clinical Endocrinology & Metabolism, (November 2004) Vol. 89, No. 11, pp. 5729-5737. print.
ISSN: 0021-972X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jan 2005
Last Updated on STN: 26 Jan 2005

AB CRH is a main regulator of the stress response. This neuropeptide and its specific receptors, CRHR-1 and CRHR-2, are disseminated throughout the central nervous system. There is a significant interspecies difference in the distribution of CRHR within the central nervous system. CRH-R1 antagonists may attenuate stress-related behavior in rats without compromising adrenal function, but few studies have addressed the same question in higher mammals. Antalarmin (AA) is a specific CRHR-1 antagonist suitable for oral administration. Social separation is a potent stressor for rhesus monkeys. Therefore, we sought to investigate the hormonal responses to chronic administration of AA using a primate stress model. Eight preadolescent (4-6 kg) male rhesus monkeys received AA (20 mg/kg.d) or placebo (PBO) orally. All animals were on a regular day/light cycle and were fed with standard monkey chow daily. The study (114 d) was comprised of the following consecutive phases: adaptation, baseline, separation (stress), recovery, and cross-over. During social separation, solid panels separated the individuals. Cerebrospinal fluid

(CSF) and femoral venous blood samples were obtained once a week on the fourth day of separation under ketamine anesthesia. Serum samples were also obtained 1 and 2 h after separation. CSF samples were assayed for CRH, AA, norepinephrine (NE) and epinephrine (EPI). Plasma was assayed for ACTH, cortisol, NE, and EPI. AA was detected in the plasma of each monkey while they were taking the active drug and in none of the animals on PBO. Among the behaviors assessed, environmental exploration, a behavior inhibited by stress, was increased during AA administration. However, AA at this dose did not affect other anxiety-related behavioral end points, including self-directed behavior, vocalization, or locomotion. We also observed that: 1) ACTH decreased between adaptation and baseline, indicating that the animals had adjusted to the novel environment; 2) ACTH and cortisol increased significantly after social separation, indicating that social separation was an adequate model for acute stress; 3) NE and EPI increased significantly during acute stress in the AA and PBO groups (P 0.005, NE; P 0.001, EPI); 4) after chronic stress, by d 4 of separation, ACTH levels were no longer significantly different from baseline, and NE and EPI remained slightly elevated when compared with baseline (P 0.05, NE; P 0.01, EPI); and 5) all the animals remained healthy and gained the expected weight during the study. In summary, oral chronic administration of a specific CRH-R1 antagonist to rhesus monkeys does not blunt the sympathoadrenal response to stress while increasing environmental exploration, a behavior that is normally suppressed during stressful events. Taken together, these findings suggest that CRHR-1 antagonists may be a valid treatment for stress-related disorders.

L5 ANSWER 9 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:298803 BIOSIS
DOCUMENT NUMBER: PREV200510085563
TITLE: Analysis of CRHR1, CRHR2 and CRHBP genes in depression and their role in the outcome of depressive episodes treated with SSRIs.
AUTHOR(S): Papiol, S. [Reprint Author]; Gutierrez, B.; Arias, B.; Catalan, R.; Gasto, C.; Gonzalez, N.; Fananas, L.
CORPORATE SOURCE: Univ Barcelona, Fac Biol, Dept Biol Anim, Unitat Antropol, Barcelona, Spain
SOURCE: American Journal of Medical Genetics, (SEP 15 2004) Vol. 130B, No. 1, pp. 163-164.
Meeting Info.: 12th World Congress of Psychiatric Genetics. Dublin, IRELAND. October 09 -13, 2004. Int Soc Psychiat Genet.
ISSN: 1552-4841 (print). E-ISSN: 1552-485x (electronic).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2005
Last Updated on STN: 15 Aug 2005

L5 ANSWER 10 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:25868 BIOSIS
DOCUMENT NUMBER: PREV200400024262
TITLE: CLOSTRIDIUM DIFFICILE TOXIN A AND PROINFLAMMATORY CYTOKINES STIMULATE CORTICOTROPIN-RELEASING
HORMONE RECEPTOR 2 (CRHR2)
EXPRESSION IN HUMAN COLONIC EPITHELIAL CELLS. .
AUTHOR(S): Anton, Pauline M. [Reprint Author]; Pan, Amy; Savidge, Tor; Newman, Paul; Simeonidis, Simos; Karalis, Katia; Pothoulakis, Charalabos
CORPORATE SOURCE: Boston, MA, USA
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 75. e-file.
Meeting Info.: Digestive Disease 2003. FL, Orlando, USA.

May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 31 Dec 2003
Last Updated on STN: 31 Dec 2003

AB Background and Objectives: We recently reported that CRH receptor antagonists inhibit C. difficile toxin A-induced diarrhea and inflammation. We also found increased expression of CRH and its CRH receptor 2 (CRHR2) in mouse intestine during toxin A-induced enteritis, and localization of this receptor on epithelial and lamina propria cells. Previous studies also indicated that the pro-inflammatory activity of toxin A is linked to the release of cytokines such as TNFalpha and IL1beta. The aims of this study were to examine whether human colonic epithelial cells express CRHR2 mRNA and study regulation of receptor expression by toxin A and proinflammatory cytokines in vitro and in vivo. Methods: RNA was purified from HT29 cells exposed to toxin A (3 mug/ml), IL-1beta or TNFalpha (10 mug/ml) for 1-24 hr. Quantitative PCR of reversed transcribed cDNA was performed using specific primers for the human CRHR2 mRNA and values were corrected by concomitant 18S cDNA amplification. Human intestinal xenografts were generated in scid mice by xenotransplantation of human fetal intestine for 10 weeks. Intestinal xenografts were injected intra-lumenally with toxin A (10 mug) for 6 hrs, and epithelial-specific expression of human CRHR2 was assessed using laser capture microdissection and real-time PCR. Results: We found that under basal conditions CRHR2 expression is very low in HT-29 cells. Stimulation of HT-29 cells with toxin A significantly increased CRHR2 expression with a peak response (10-fold increase) 1 hr and still evident for up to 24 hrs following its application. Furthermore, CRHR2 mRNA expression was induced in HT-29 cells stimulated with IL1beta and TNFalpha for 3 hrs. Moreover, a significant induction of epithelial-derived CRHR2 mRNA was recorded following toxin A inoculation of human intestinal xenografts in vivo (1.18 (control) vs 3.74 (toxin A)). Summary & Conclusion: These are the first results to demonstrate CRHR2 expression in human colonocytes, and its upregulation by a bacterial exotoxin and by proinflammatory cytokines. We speculate that CRH released in the intestine during C. difficile infection stimulates fluid secretion and inflammation by interacting with this receptor on colonocytes and lamina propria macrophages. Supported by the National Institutes of Health (DK 33506) and the Crohn's and Colitis Foundation of America, Inc..

L5 ANSWER 11 OF 14 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:151102 BIOSIS

DOCUMENT NUMBER: PREV200200151102

TITLE: Functional expression of corticotropin-releasing hormone (CRH) receptor 1 in cultured rat microglia.

AUTHOR(S): Wang, Wei; Ji, Ping; Riopelle, Richard J.; Dow, Kimberly E. [Reprint author]

CORPORATE SOURCE: Department of Pediatrics, Kingston General Hospital, Doran 3, Room 6-303, Kingston, Ontario, K7L 2V7, Canada
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SOURCE: Journal of Neurochemistry, (January, 2002) Vol. 80, No. 2, pp. 287-294. print.
CODEN: JONRA9. ISSN: 0022-3042.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Feb 2002
Last Updated on STN: 26 Feb 2002

AB Corticotropin-releasing hormone (CRH), known as a key regulator of the

hypothalamic-pituitary-adrenal axis response to stress, elicits its biological effects by binding to two membrane receptors (CRH-R1 and CRH-R2). The present studies examined the presence of functional expression of CRH receptors in cultured microglia of rat. CRH-R1 mRNA and protein were detected by reverse transcriptase polymerase chain reaction (RT-PCR), western blotting and receptor chemical cross-linking assay in cultured microglia. CRH-R2 mRNA was undetectable by RT-PCR. The radioligand binding analysis using (125I)Tyr-rat/human CRH revealed a high affinity binding site (Kd of 1..2 nM and Bmax of 84 fmol/mg of protein). Competition studies using CRH and related peptides indicated kinetic and pharmacological characteristics consistent with the CRH-R1 receptor subtype. Receptor chemical cross-linking assay demonstrated a single band of CRH receptor with a molecular weight of apprx77 kDa, which was inhibited in the presence of excess unlabeled rat/human CRH in a dose-dependent manner and inhibited by a CRH receptor antagonist astressin. Functional coupled cAMP production in cultured microglia was stimulated by exogenous addition of CRH and related peptides in a dose-dependent manner and blocked by astressin. Our findings suggest the functional expression of CRH-R1 receptor in rat microglia, indicating an important mechanism of interaction between immune and neuroendocrine systems in brain physiological and pathological conditions.

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ACCESSION NUMBER: 2003:304782 BIOSIS
DOCUMENT NUMBER: PREV200300304782
TITLE: UROCORTIN II AND III INHIBIT ESTROUS BEHAVIOR IN SYRIAN HAMSTERS.
AUTHOR(S): Seymour, P. L. [Reprint Author]; Jones, J. E. [Reprint Author]; Wade, G. N. [Reprint Author]
CORPORATE SOURCE: Center for Neuroendocrine Studies, University of Massachusetts, Amherst, MA, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 482.14. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jul 2003
Last Updated on STN: 2 Jul 2003

AB Corticotropin-releasing hormone (CRH) receptor ligands such as CRH and urocortin inhibit estrous behavior in steroid-primed Syrian hamsters when infused intracerebroventricularly (ICV) 30 min prior to behavioral testing. At low doses (0.1 nmol) this inhibition lasts less than 4 hr. Conversely, the CRH receptor antagonist, astressin, reverses the inhibition of estrous behavior by food deprivation and by ICV infusion of neuropeptide Y. Furthermore, astressin treatment also induces sexual receptivity in nonresponders, animals that do not normally come into heat when treated with hormones, and this effect persists in subsequent weekly tests in the absence of any further astressin treatment. Because CRH, urocortin, and astressin all bind to both types of CRH receptors (CRH-R1 and -R2), this work does not speak to the identity of the endogenous ligand(s) which inhibit female sexual behavior via CRH receptors, nor does it provide any information about the receptor type(s) involved. To begin to address this question, we examined the effects of two CRH-R2 agonists, urocortin II and urocortin III, on estrous behavior in ovariectomized, steroid-primed hamsters. Both urocortins, infused ICV 30 min prior to behavioral testing, inhibited estrous behavior.)Urocortin II was as effective as urocortin and significantly more effective than urocortin III at inhibiting lordosis. The relative potency of the three

urocortins is consistent with their affinities for the CRH-R2. These data suggest that the inhibitory effects of CRH receptor agonists on female sexual behavior are mediated by CRH-R2.

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ACCESSION NUMBER: 2002:175780 BIOSIS
DOCUMENT NUMBER: PREV200200175780
TITLE: Corticotropin releasing hormone (CRH) is a proinflammatory peptide in mouse ileum.
AUTHOR(S): Wik, Michael [Reprint author]; Wang, Chi; Venichaki, Maria; Kuhnt-Moore, Sabina; Zhao, Dezheng; Zacks, Jeff; Liu, Jennifer; Karalis, Katia; Pothoulakis, Charalabos
CORPORATE SOURCE: Beth Israel Deaconess Medical Ctr and Harvard Medical Sch, Boston, MA, USA
SOURCE: Gastroenterology, (April, 2001) Vol. 120, No. 5 Supplement 1, pp. A.38-A.39. print.
Meeting Info.: 102nd Annual Meeting of the American Gastroenterological Association and Digestive Disease Week. Atlanta, Georgia, USA. May 20-23, 2001. American Gastroenterological Association; American Association for the Study of Liver Diseases; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Mar 2002
Last Updated on STN: 6 Mar 2002

L5 ANSWER 14 OF 14 MEDLINE on STN

ACCESSION NUMBER: 2000206568 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10742109
TITLE: Deletion of crhr2 reveals an anxiolytic role for corticotropin-releasing hormone receptor-2.
AUTHOR: Kishimoto T; Radulovic J; Radulovic M; Lin C R; Schrick C; Hooshmand F; Hermanson O; Rosenfeld M G; Spiess J
CORPORATE SOURCE: Howard Hughes Medical Institute, Department and School of Medicine, University of California, San Diego, La Jolla, CA, USA.
SOURCE: Nature genetics, (2000 Apr) Vol. 24, No. 4, pp. 415-9.
Journal code: 9216904. ISSN: 1061-4036.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 12 May 2000
Last Updated on STN: 12 May 2000
Entered Medline: 4 May 2000

AB Corticotropin-releasing hormone (Crh), a 41-residue polypeptide, activates two G-protein-coupled receptors, Crhr1 and Crhr2, causing (among other transductional events) phosphorylation of the transcription factor Creb. The physiologic role of these receptors is only partially understood. Here we report that male, but not female, Crhr2-deficient mice exhibit enhanced anxious behaviour in several tests of anxiety in contrast to mice lacking Crhr1. The enhanced anxiety of Crhr2-deficient mice is not due to changes in hypothalamic-pituitary-adrenal (HPA) axis activity, but rather reflects impaired responses in specific brain regions involved in emotional and autonomic function, as monitored by a reduction of Creb

phosphorylation in male, but not female, Crhr2-/- mice. We propose that Crhr2 predominantly mediates a central anxiolytic response, opposing the general anxiogenic effect of Crh mediated by Crhr1. Neither male nor female Crhr2-deficient mice show alterations of baseline feeding behaviour. Both respond with increased edema formation in response to thermal exposure, however, indicating that in contrast to its central role in anxiety, the peripheral role of Crhr2 in vascular permeability is independent of gender.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	89.47	89.68

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jan 4, 2008 (20080104/UP).